

10/058,903

-2-

A0000513-01-AWZAWZ

REMARKD/ARGUMENTS**35 U.S.C. 103(a) Rejection**

Claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pande (US Patent 6359005) in view of Wirth et al. (J. Pharm. Sci., 87(1), 31-39, 1998). In the present application, Applicants claim a group of novel compounds useful for treating certain disorders. The structures of some of these compounds are provided on pages 6-9 of the application. Applicants teach that these novel compounds can be made with two known starting materials, pregabalin and lactose, by known methodologies, including Maillard reaction. Applicants do not claim the synthesis process. In rejecting the claims, the Examiner alleges that "[s]ince Pande teaches the pregabalin, its derivatives, and pharmaceutically acceptable salts for use in the treatment of anxiety or epilepsy (nervous system disorder), and Wirth et al., teach the excellent compression and stability characteristics of lactose and its ability to undergo Maillard reactions to produce formulation, one skilled in the art would have a reasonable expectation for success in combining both references to accomplish the pregabalin lactose conjugate, its pharmaceutical composition and their use in the treatment of anxiety or epilepsy." The Examiner goes on to state, "The motivation for doing so is provided by Pande, which suggests the use of pregabalin in the treatment of anxiety or epilepsy because of the nontoxic nature of the compound, ease of preparation and the ease of administration of the drug (see col. 3, lines 55-60)." Applicants respectfully traverse the rejection, for reasons detailed below.

First, applicants respectfully submit that the claimed compounds are not taught or suggested by the reference, individually or in combination. Pande teaches pregabalin, one of the starting materials that can be used to make the compounds of the inventions. Although the structure of pregabalin can be traced in the structures of compounds of the invention, a comparison of the structure of pragabalin with the overall structures of the compounds of the invention immediately reveals a striking and distinct difference between them, with the pregabalin-like structure being an insignificant physical portion of the overall structures of the

10/058,903

-3-

A0000513-01-AWZAWZ

claimed compounds. Because of such striking, distinct structural difference, the compounds of the invention could not have been obvious to a person skilled in the art in view of Pande.

Wirth, et al. teach that lactose, the other starting material for making the compound of the invention, can undergo Maillard reaction with fluoxetine hydrochloride. It is Applicants' position that Wirth et al at best teach the process that can be utilized to make the compounds of the inventions, but Wirth do not teach the compounds, the claimed subject matter of the application, and therefore, can not render the claimed compounds obvious. The other starting material used in Wirth et al is fluoxetine chloride. Fluoxetine chloride has no structural similarity at all to either pregabalin or the compounds of the inventions. The end products of the Maillard reaction disclosed in Wirth are also strikingly different in structures from the compounds of the invention. Because of such striking, distinct structural differences, the compounds of the invention could not have been obvious to a person skilled in the art in view of Wirth et al. It is immaterial that Wirth discloses the process of Maillard reaction with lactose, because the present application does not claim the process of making the compounds of the invention.

Second, applicants respectfully submit that there is no basis in either reference itself for combining them to arrive at the claimed invention. As the Court of Appeals for the Federal Circuit mandates, obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching, suggestion or inventive supporting the combination. Further, the teaching can not be taken from the applicant's own disclosure, and it is impermissible to use hindsight occasioned by the applicant's teaching to hunt through the prior art for the claimed elements and combine them as claimed. In re Zurko, 111 F. 3rd 887, 42 USPQ2d 1476 (Fed. Cir. 1997). In the present application, applicants' own disclosure teaches a process of making the compounds of the invention, that is by Maillard reaction with lactose and pregabalin. As explained above, while Wirth et al disclose such a reaction with lactose and fluoxetine, they do not suggest the compounds of the invention themselves. As also explained above, Pande teaches pregabalin, which is distinctly and strikingly different in structure from the compounds of the invention. Similarly, fluoxetine

10/058,903

-4-

A0000513-01-AWZAWZ

chloride or the end products disclosed in Wirth et al has no structural similarity at all to either pregabalin or the compounds of the inventions. Because of such striking, distinct structural differences, neither reference suggests the combination of the reference to arrive at the compounds of the invention. Further, in addition to the Maillard reaction of lactose and fluoxetine, Wirth et al also suggest that lactose can undergo Maillard reaction with possibly an infinite number of other starting compounds to produce an infinite number of different end products. It follows that it may possible that pregabalin can be one of the infinite number of starting materials in the Maillard reaction, or possible that the compounds of the inventions can be some of the end products of the Maillard reaction, and thus it may be obvious to try the combination. However, "obvious to try" is not the stand of 35 U.S.C. 103. There is no teaching in either reference that would point to the compounds of the invention.

Applicants further submit that neither reference provides motivation to combine the references to arrive at the claimed invention. The Examiner states that the motivation to combine comes from Pande "which suggests the use pregabalin in the treatment of anxiety or epilepsy of the nontoxic nature of the compound, ease of preparation and the ease of administration of the drug (see col. 3, lines 55-60)." Applicants respectfully disagree. As explained above, pregabalin is distinctly different in structure from the compounds of the invention. While Pande teaches that pregabalin is useful for treating certain disorders, and has desirable properties, it provides no motivation to a person skilled in the art to combine pregabalin with lactose in a Maillard reaction to produce compounds that are totally different in structures from pregabalin. Further, according to Wirth et al, formation of the Maillard reaction products with lactose and fluoxetine is an indication of instability of the formulation, which is undesirable for any pharmaceutical products. Wirth at al further state that the clinical significance of the fluoxetine-lactose interaction is unknown. Taken together, this also weighs against a finding of a motivation to make the claimed compounds.

10/058,903

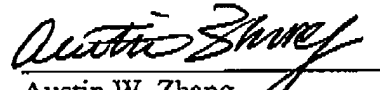
-5-

A0000513-01-AWZAWZ

For at least the above reasons, Applicant respectfully submit that the claimed invention would not be obvious over Pande in view of Wirth et al. Consequently, Applicants requests that the rejections to the claims be withdrawn, and timely Notice of Allowance be issued in this case.

Respectfully submitted,

Dated: 12/19/2003


Austin W. Zhang
Registration No. 48,061
Warner-Lambert Company
2800 Plymouth Road
Ann Arbor, MI 48105
Telephone: (734) 622-5035
Facsimile: (734) 622-1553